

DETAILED ACTION

Applicants' request for continued examination of October 13, 2011, in response to the action of April 14, 2011, is acknowledged. It is acknowledged that no claims have been cancelled, amended, or added. Claims 46-55 and 58-64 are pending. The elected invention is directed to the protease polypeptide of SEQ ID NO: 2 and variants thereof. Claim 61 was previously withdrawn as being directed to non-elected subject matter. Claims 46-55, 58-60, and 62-64 are encompassed by the elected invention, directed to the protease polypeptide of SEQ ID NO: 2, and are hereby reexamined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 46-55, 58, 59, and 62-64 under 35 U.S.C. 102(b) as being anticipated by Isono et al, 1972 as evidenced by Isono et al, 1972 and Esaki et al, 1994 for the reasons explained in the prior actions, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. These arguments are not found to be persuasive for the reasons following each argument.

(A) As set forth in the Supplemental Knotzel Declaration, "the concentration of LAS detergent in the assay experiments carried out under my direction and supervision is the same as the concentration of LAS detergent in the assay experiments of Isono." Supplemental Knotzel Declaration, ¶5. In particular, the final concentration of the assay performed according to the experiments of the January 2011 Knotzel Declaration is 0.0625% (0.625mg/ml) LAS, and the final concentration of the assay reported in Example

4 of Isono is also 0.0625% (0.625mg/ml) LAS (i.e., 5 mg of 25% LAS solution taken in 2 mL of buffer).

Supplemental Knotzel Declaration, ¶3-4.

(A) Reply: The Supplemental Knotzel Declaration of October 13, 2011 is acknowledged.

However, said declaration does not persuade the Examiner that the experiments disclosed by the January 2011 Knotzel Declaration were performed with the same concentration of detergent used by Isono et al.

The Supplemental Knotzel Declaration of October 13, 2011 states:

“LAS-detergent (Detergent 1) was prepared according to Table 1 of Isono as follows:

25% LAS: 274.7mg/ml

40% Sodium tri-phosphate: 400mg/ml

29% Sodium sulphate: 290mg/ml

5% Sodium silicate: 50mg/ml

1% Carboxymethyl cellulose (Finnfix BDA): 10mg/ml

However; these amounts of solid ingredients were undissolvable in 100mL of 0.05M Tris-HCl pH 11 buffer. For this reason, the above listed ingredients were combined and diluted 10- fold so that oil solids would dissolve. This gave a stock of 2.5% (27.47mg/ml) LAS solution.

For the assay, the 2.5% (27.47mg/ml) LAS solution is further diluted according to Isono, but in order to achieve the same final dilution of LAS-detergent as Isono, we had to use 10 times more of our stock. 500mg of 2.5% LAS solution is taken in 20 mL 0.05 TRIS-HCl pH 11. This gives a final concentration of 0.0625% (0.625mg/ml) LAS as final concentration of the assay.”

Based on the above, the following is assumed. That, Applicants first made a stock solution comprising 27.47mg/ml LAS detergent. Subsequently, said stock solution was diluted by adding 500μl [ie not mg] of the stock solution (comprising 27.47mg/ml LAS) into 20ml of buffered Tris/HCl. The resulting diluted solution comprised 0.625mg/ml LAS.

(B) Isono reports preparation of a 25% LAS solution (250mg/ml), 5 mg of 25% LAS solution is taken into 2mL of buffer to provide 0.0625% (0.625mg/ml) LAS as final concentration of the assay.

(B) Reply: As explained in the prior action, Isono et al used a final concentration of 2.5 mg/ml LAS detergent. Isono et al specifically teaches (Example 6):

“In the same manner as in Example 1, several microorganisms belonging to the genus *Fusarium* and the genus *Gibberella* are cultivated for 6 days.

The cultures are then centrifuged to give supernatant fluids which are used as enzyme solutions. To 2,000 parts by volume each of the enzyme solutions are added 5 parts by weight of the LAS-detergent described in Example 4, and protease activity of the resulting solution is determined by the specified assay method. The results are set forth in Table 5 indicating that the LAS-detergent does not inhibit any activity of the enzymes produced by those alkali protease-producing microorganisms.”

Thus, Isono et al dissolved the ratio of 5 parts of LAS (5gms) into 2000 parts (2000ml) of supernatant enzyme solution for a final concentration of 2.5mg/ml LAS. Table 5 of Example 6 shows that the total protease activity of the *Fusarium solani* supernatant solution was unaffected by 2.5 mg/ml LAS.

For these reasons and those explained in the prior actions, the experiments disclosed by the January and August 2011 Knotzel Declarations were not performed with the same concentration of LAS detergent used by Isono et al.

Moreover, the lack of an effect of 2.5 mg/ml LAS on the total protease activity in the *F. solani* culture supernatant does not provide prima facie evidence that there is not, in said supernatant, a limited amount of the protease of SEQ ID NO: 2, which is inhibited by 0.625mg/ml LAS.

(C) In direct contrast, as determined in the January 2011 Knotzel Declaration, the *F. solani* protease of SEQ ID NO: 2 has essentially no activity in the presence of the LAS-detergent of Isono et al. In other words, the LAS-detergent of Isono et al inhibits any activity of the claimed trypsin-like protease.

(C) Reply: See Reply (A) and (B), above.

(D) If Applicants' claimed protease was a component of Isono et al.'s material, as the Examiner alleges, Isono et al.'s material would have lost at least some activity in the presence of LAS-detergent, since Applicants' enzyme is not active in the specific LAS-detergent composition according to Isono et al. However, as Isono et al. states, the LAS-detergent does not inhibit any activity of the enzymes

produced. Accordingly, whatever it was that Isono et al. assayed, it did not include Applicants' claimed trypsin-like protease of SEQ ID NO: 2.

(D) Reply: The lack of an effect of LAS on the total protease activity in the *F. solani* culture supernatant does not provide prima facie evidence that said supernatant does not comprise a limited amount of the protease of SEQ ID NO: 2 such that its inhibition by LAS does not significantly affect the total level of protease activity in the supernatant.

For these reasons and those stated in the prior actions, rejection of Claims 46-55, 58, 59, and 62-64 under 35 U.S.C. 102(b) as being anticipated by Isono et al, 1972 as evidenced by Isono et al, 1972 and Esaki et al, 1994, is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection of Claim 60 under 35 U.S.C. 103(a) as being unpatentable over Isono et al, 1972 in view of Okuda et al, 2004 (FD 12-MAR-2003), for the reasons explained in the prior actions, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. These arguments are not found to be persuasive for the reasons stated in each reply.

(A) As explained in detail above, Isono et al. does not teach or suggest the claimed proteases.

(A) Reply: See the replies above.

(B) Hastrup et al. discloses proteases. However, Hastrup et al. does not disclose Applicants' claimed proteases, and does not teach or suggest detergent compositions comprising the proteases of the present invention, either alone or in combination with Isono et al. and/or Okuda et al.

(B) Reply: There is no use of "Hastrup et al" for the instant rejection.

(C) Okuda et al. disclose a detergent composition comprising an alkaline protease and one or more other enzymes. However, Okuda et al. does not teach or suggest detergent compositions comprising the proteases of the present invention, either alone or in combination with Isono et al. and/or Hastrup et al.

(C) Reply: See the action of September 18, 2009, Reply (A); p6.

For these reasons and those stated in the prior actions, rejection of Claim 60 under 35 U.S.C. 103(a) as being unpatentable over Isono et al, 1972 in view of Okuda et al, 2004 (FD 12-MAR-2003), is maintained.

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

It is suggested that Applicants' representative contact the Examiner to discuss this application.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for

extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN SWOPE whose telephone number is 571-272-0943. The examiner can normally be reached on 11a-7:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
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